

The μ ChemLabTM project: micro total analysis system R&D at Sandia National Laboratories

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Background

Sandia National Laboratories¹ is one of the US Department of Energy multi-program laboratories. The organization operates two major R&D facilities, one in Albuquerque, New Mexico, and the other in Livermore, California, as well as a number of test ranges and smaller facilities. Sandia is engaged in a spectrum of different activities ranging from basic energy research to systems engineering to manufacturing operations for a variety of sponsors, but the major part of the laboratories' work is driven by the needs of national security. To meet its mission needs, Sandia has a long established expertise in microelectronics and photonics² and has built upon this capability to explore and apply microelectromechanical systems^{3,4} (MEMS). In addition, Sandia has an established expertise in fluidics and in advanced laser-based diagnostics.⁵ In 1996, a diverse group of staff associated with these established operations proposed that Sandia mount an initiative to apply facets of these capabilities to development and demonstration of micro total analysis systems (μ TAS) for use in applications of interest to national security. This initiative was funded beginning in 1997 under the name ' μ ChemLab'.

By 1996, workers in many institutions throughout the world had demonstrated the laboratory feasibility of μ TAS. This work had also underscored the potential advantages to be realized through miniaturization of chemical analysis systems: speed, high sensitivity, low reagent requirements, portability, and low cost. Consequently, at Sandia, the μ ChemLab project was to focus on two

key objectives: application to issues of national security and the demonstration of complete μ TAS systems. Two target analysis applications were defined for the project: detection and analysis of chemical warfare agents and detection of low levels of explosives contamination in soils. The first application is of obvious national security interest; the second was motivated by the need for rapid, easy-to-use analytical methods for use in operations involving cleanup and conversion of sites that had been used for military purposes during the Cold War.

Definition of target demonstration applications highlighted the fact that sensitive, field portable, easy-to-use chemical analysis systems could be used in a very wide variety of different applications. This reinforced a belief that flexibility was a key requirement for these types of analytical systems and underscored a desire to approach the development of such instruments through the miniaturization of 'known' general chemical analysis systems. The application space would also require the ability to analyze both gaseous and liquid samples. The approach adopted was to miniaturize both gas and liquid separations systems to provide a robust, well understood, and flexible miniaturized chemical analysis platform. Specific analytical methods would be developed and demonstrated to illustrate the application of these μ TAS instruments to specific problems of interest (understanding that extension to additional analysis problems would 'only' require development of additional analytical methods for use on the miniaturized platform). Finally, since the ultimate user of these systems was envisioned to be someone without specific training or

expertise in chemical analysis, it would be essential to ensure that these μ TAS instruments would be relatively easy to use. That is, the goal was to use the power and flexibility of chemical chromatography and electrophoresis while hiding the complexities from the ultimate user.

By late 1997, growing concerns about possible terrorist attacks with chemical or biological agents led to establishment of the Chemical & Biological National Security Program⁶ (CBNP) within the US DOE. The mission of this Program is to 'develop, demonstrate and deliver technologies and systems that will lead to major improvements in the US capability to prepare for and respond to chemical or biological attacks.' One objective of this Program is development of sensor systems that could be used by emergency personnel, first responders, during a suspected terrorist attack. Funding from this Program has been critical to extending μ TAS R&D at Sandia and resulted in an additional demonstration analytical problem for the μ ChemLab project—detection and analysis of biotoxins.

Technical overview

Evaluation of the demonstration analysis problems underscored that a μ ChemLab system would need to fulfil a variety of different requirements: high sensitivity—ppb detection levels would be required for analysis of chemical warfare agents or biotoxins; rapid response (~ 1 min); low false alarm rates; good immunity to potential background interference; low power requirements; and low cost.

As systems concepts were developed (Fig. 1), a variety of features or approaches were included to help meet these requirements. For instance, preconcentrators were included in gas analysis systems to improve sensitivity and to reject potential interferents. To reduce false alarm rates, analysis architectures rely on independent parallel analysis and/or detection channels. Other features were included to reduce power requirements and ultimate systems cost.

Chemlab systems consist of several major subsystems. These include chemical analysis (both gas and liquid subsystems have been developed), control, power supply, and data acquisition. Chemical analysis subsystems are further divided by sample collection and preconcentration, separation, and detection functions.

The μ ChemLab gas analysis subsystem^{7,8} is designed around a microfabricated sample collector/preconcentrator, a micromachined chromatography column, and a set of surface acoustic wave (SAW) detectors. The preconcentrator⁹ uses a thermally isolated microfabricated membrane with a resistive heater. The membrane is coated with a microporous sol-gel material that is tailored to collect species of interest while rejecting (background) concentrations of other chemicals. Because of the low thermal mass of these devices, they can be rapidly heated (to 200 °C in ≤ 10 ms), resulting in rapid desorption of adsorbed species and providing a well-defined sample pulse that is introduced onto the separation column. The GC column used in μ ChemLab is typically a spiral channel fabricated in a silicon substrate by deep reactive ion etching. Typical column dimensions are 40–80 μ m wide by 250 μ m deep. Columns 1 m in length are fabricated in a device of 1 cm² area. These columns can

be coated with a stationary phase and they can be thermally ramped to facilitate chemical separations. Finally, detection at the column outlet is accomplished using SAW detectors coated with chemically selective coatings. Polymer coatings used to detect chemical warfare agents were developed by Jay Grate of the Pacific Northwest National Laboratory. Fig. 2 provides a sense of the size scale of these various devices.

The liquid analysis subsystem¹⁰ used is comprised of two major elements: a separations column (or series of parallel columns) and a detector. Separations columns are typically fabricated by etching microchannels in either a glass or a fused silica substrate. Several different separations methods have been used on chip (depending on the analysis objectives) and many others have been demonstrated. For analysis of explosives in soils, the chemical separation method used is micellar electrokinetic chromatography¹¹ (MEKC). For detection and analysis of biotoxins, two parallel separations methods are currently being used: capillary zone electrophoresis (CZE)

and capillary gel electrophoresis (CGE). In each of these cases, detection is accomplished with laser induced fluorescence (LIF), which was selected because of the high sensitivities possible with this technique. For analysis of explosives, the detection system is designed around a microfabricated vertical cavity surface emitting laser (VCSEL) operating at 750 nm.¹² In this case, indirect LIF is used, and the selected wavelength allows glass to be used as the chip substrate (Fig. 3). For the analysis of protein biotoxins, indirect LIF at IR wavelengths was not feasible, so detection is accomplished by labeling the proteins with a fluorescent tag and detecting the analytes with LIF with a 392 nm excitation wavelength. Operation at this wavelength requires use of fused silica substrates, since glass background fluorescence is too high. Further, VCSELs are not available at such short wavelengths, so conventional laser diodes must be used, requiring a more complex (and larger) optical system. Figs. 4 and 5 show the liquid analysis subsystem for the biotoxins analyzer. Work with early designs of these systems revealed that reproducibility from run to run was poor. This problem was traced to microionic effects in buffer reservoirs and sample loops. To deal with this problem, reservoir and electrode designs that are immune to it have been developed and are now in use.¹¹

While the chip based chemical analysis subsystems are clearly at the heart of these devices, significant development work has been required to produce the other subsystems. For example, to allow for use of SAW detectors in a low power/low noise environment, novel excitation electronics designs were required. To allow automated operation of the liquid analysis system, it was necessary to design compact,

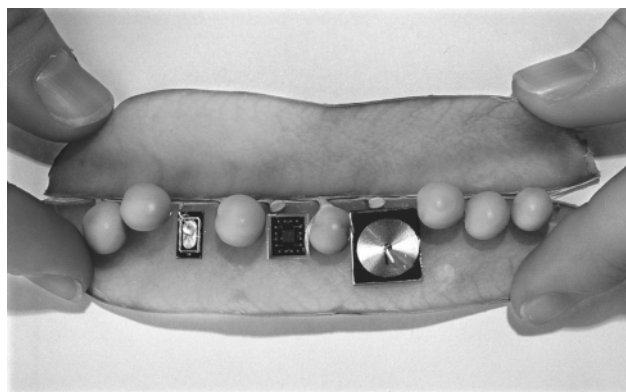


Fig. 2 Components of the μ ChemLab gas analysis subsystem—from left to right the SAW detector (an array of four), the sample collector/preconcentrator, and a 1 m gas chromatography column.

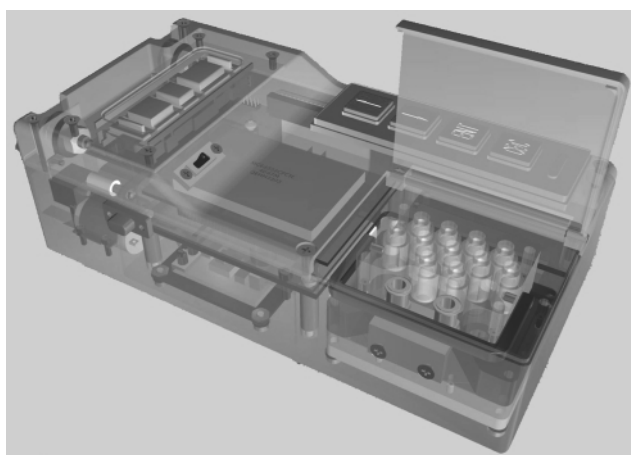


Fig. 1 CAD layout of the μ ChemLab system prototype.

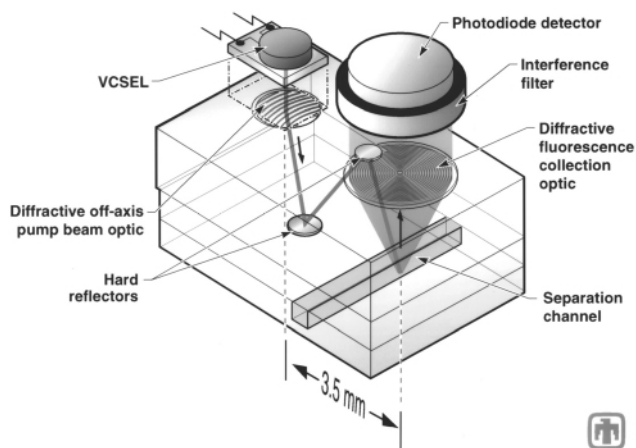


Fig. 3 Microfabricated indirect LIF detection system used in the μ ChemLab explosives analyzer.

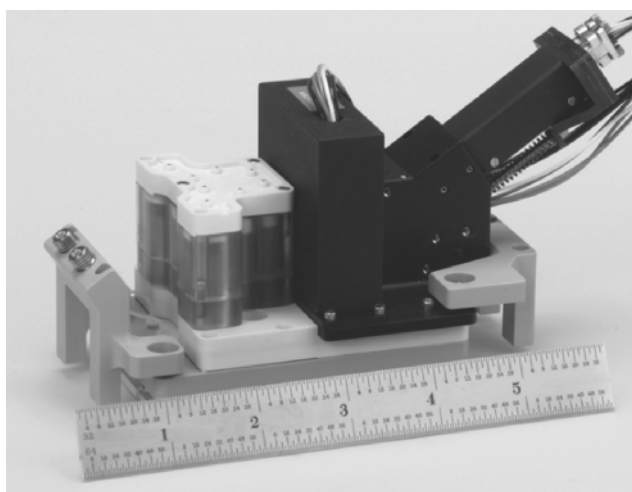


Fig. 4 Liquid analysis subsystem from the biotoxins analyzer. Injection ports to the left. Buffer and waste reservoir cartridge in the center. LIF detection subsystem to the right. The separations chip is underneath.

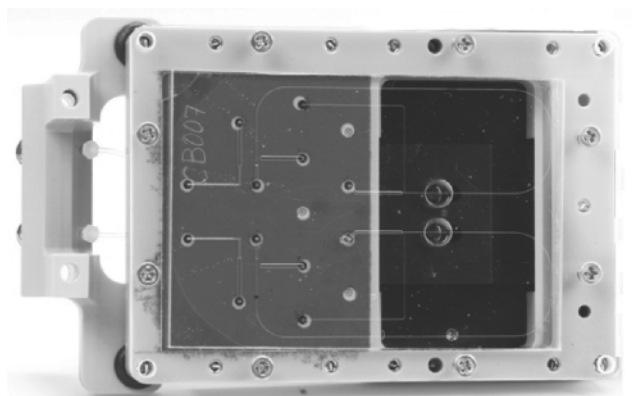


Fig. 5 Carrier mounted dual column (CZE and CGE) separations chip used in biotoxins analysis.

multichannel, computer-controlled, kV switching systems.

Status

Research prototype μ ChemLab systems are now being evaluated under laboratory conditions (Figs. 6 and 7).

Initial test results with these instruments began in Fall 2000, and they show considerable promise.^{9,10} For example, tests with instruments configured for analysis of chemical warfare agents (Fig. 8) show very rapid analysis times, high sensitivity, and good immunity to potential background

interference. Similar benefits are possible for analysis of liquids as demonstrated in tests with the biotoxins analyzer (Fig. 9).

After the initial series of tests (with thousands of different runs), a number of deficiencies or problems with each of these instruments was identified. This has led to redesign of various components and subsystems to correct these problems and to improve device performance and utility. These second generation instruments are now available and testing will soon begin. Tests now planned include limited field trials under relatively mild environmental conditions.

The scope of analytical applications for these devices is also being explored and expanded. For example, rapid analysis of gaseous hydrocarbon mixtures has been demonstrated,⁷ along with a variety of other applications. One of the most exciting results that has come of this work is the development of a method to produce high hydrostatic pressures on chip.¹³ This has led to a demonstration of chip based high-performance liquid chromatography (HPLC) and opened that suite of analytical methods to chip-based approaches. Work continues to implement HPLC in μ ChemLab systems.

In an effort to provide tools to facilitate design of these microfluidic systems, a significant amount of work at Sandia has been directed at development of analytical tools to be used in component design.^{14,15} This work has led to the development of specific design rules and to design codes of use in optimization of microfluidic components for lab on chip systems.

Future directions

The ultimate objective of this effort is to provide the technology and the feasibility demonstrations that will allow deployment of μ TAS systems tailored to specific problems of national security interest. To accomplish this objective, several different types of activities are necessary in the future. First, continued testing and design improvements are needed to demonstrate that devices of this type can be used under actual field conditions. Second, the analytical methods employed must be extended to a more comprehensive suite of agents. Finally, the technologies and processes embodied in these devices must be transferred to an appropriate commercial entity (or entities) for further development, production, marketing and customer support.

As mentioned, prototypes of these types of systems are now being prepared for



Fig. 6 Prototype μ ChemLab system. The unit shown contains both gas and liquid analysis subsystems. Simplified versions of this device (containing only the gas analysis subsystem) are now being tested.



Fig. 7 Prototype μ ChemLab liquid analysis system. This instrument is configured to analyze injected liquid samples for protein biotoxins.

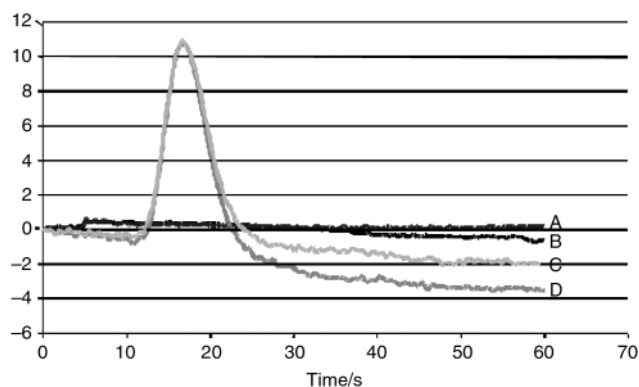


Fig. 8 Detection of Soman (a nerve agent) with a μ ChemLab system. Duplicate runs, except that in one case (line D) the gas sample contained 1% diesel fumes.

field trials. These tests will begin shortly and will provide information on how such things as environmental effects and background chemical concentrations will affect the performance of these devices. In addition, extensive testing is planned to explore issues such as reproducibility, system and component lifetimes, and failure modes. We are also working to develop 'next generation' components—improved approaches to sample handling, fluidic control and on-chip system monitoring.¹⁶

Additional analytical methods are being developed which will extend the usefulness of these instruments. For example, methods to use the gas analysis system for detection of toxic industrial chemicals (TICs), which may constitute a significant threat, are under development. Eventually, plans call for use of these systems (with appropriate methods) to detect signatures from the full range of chemical and biological threat agents, including pathogens.

It should be obvious that these instruments have potential applications well beyond detection and analysis of the chemical and biological agents that might be employed by terrorists. Sandia is now working with a number of commercial organizations to further develop and improve designs of these systems and to develop and demonstrate appropriate analytical methods to allow use of these systems and technologies in a much broader range of economically important applications.

Acknowledgements

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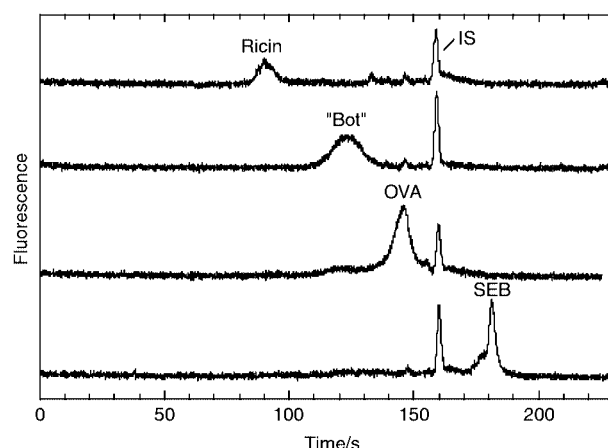


Fig. 9 Analytical runs with several different protein toxins (and simulants). IS is an internal standard; ricin and SEB (staphylococcal enterotoxin B) are toxins; ovalbumin (OVA) and 'bot' are non-toxic proteins used as simulants for other toxins.

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